

## Correspondence

# Using tacrolimus in living donor liver transplantation recipients with high model for end-stage liver disease scores might increase the risk of postoperative neuropsychologic deficits

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For decompensated liver cirrhosis and hepatocellular carcinoma, liver transplantation provides these patients the only curative treatment option with better long-term results. The Model for End-stage Liver Disease (MELD) system is a good tool to predict short-term mortality among these patients and has also been applied to allocate liver grafts to patients on waiting lists in several countries.<sup>1</sup> In 2002, the New York State Committee on Quality Improvement in Living Liver Donation prohibited live liver donation for potential recipients with MELD scores greater than 25.<sup>2</sup> Alves et al suggested MELD scores >18 was associated with higher probability of graft failure after living donor liver transplantation (LDLT).<sup>3</sup> Previous studies have demonstrated that using tacrolimus as primary immunosuppressant, neuropsychologic deficits had been found to be higher in recipients with elevated preoperative MELD scores, especially for those MELD scores greater than 15.<sup>4,5</sup> We here summarize our experiences on postoperative neuropsychologic deficits in LDLT recipients using tacrolimus with high MELD scores.

From 2004 to 2012, 218 LDLT were performed in our transplant center. Postoperative neuropsychologic deficits were observed in 8 male recipients (3.7%) during the first week, including: insomnia (2), vivid

dreams (1), paresthesias (1), anxiety (1), agitation (2), and cognitive impairment (1). The mean age was 42 (33-57) and the mean MELD score was 21 (9-28). All of the patients did not have the history of excessive alcohol use and preexisting central nervous system damage. Decompensated liver cirrhosis caused by HBV infection was seen in 5 patients, while hepatocellular carcinoma (HCC) was seen in 3 patients. Right living lobe liver transplantations were performed by the same medical team, with a mean graft to body weight ratio (GBWR) 0.78 (0.6-1.0). Our center used tacrolimus as the initial immunosuppressant for all liver transplant recipients. In the first postoperative week, the mean tacrolimus blood level was 9.3 (6.5-11.6), while the mean total bilirubin blood level was 23mmol/L (15-30mmol/L), the mean creatinine blood level was 67umol/L (45-90umol/L), and the mean serum sodium level was 139mmol/L (136-143mmol/L). The mean ICU stays was 9 days (7-12 days). After switching tacrolimus to sirolimus, all recipients were relieved from neuropsychologic deficits and discharged eventually without primary graft non-function, renal failure, acute rejection, re transplantation or death.

All the 8 recipients had a relatively higher MELD scores to other LDLT recipients. Although the mechanistic pathway resulting in these neural deficits is not clear, our hypothesis is that several reasons might contribute to it: 1) elevated preoperative MELD scores usually represents a poor liver function, potential encephalopathy risk, and increased susceptibility to blood-brain barrier disruption, associating with increased vulnerability to postoperative tacrolimus neurotoxicity; 2) when GBWR <0.8, a small-for-size (SFS) living graft recipients have significantly decreased tacrolimus dosage requirements compared with non-SFS grafts recipients in LDLT. A regular dosage may cause higher tacrolimus blood levels in these SFS graft recipients and elevated blood levels of tacrolimus are associated with neurotoxicity<sup>6</sup>; 3) in order to ensure the donor safety, a SFS graft may be transplanted to a high MELD recipient. This interaction may apparently increase the postoperative neuropsychologic deficits risk in such group of patients.

Although the switching from tacrolimus to sirolimus can effectively relieve patients' neuropsychologic deficits, there are potential risks in graft primary non-function, infection, and

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acute rejection. Postoperative neuropsychologic deficits should be paid more attention when LDLT is performed for high preoperative MLED scores recipients. A lower tacrolimus dosage or a sirolimus-based immunosuppressant may decrease such risk.

**KEY WORDS:** Neuropsychologic deficits, Model for end-stage liver disease score, Living donor liver transplantation, Tacrolimus.

**Abbreviation:** MELD: Model for End-stage Liver Disease; LDLT: living donor liver transplantation; HCC: hepatocellular carcinoma; GBWR: graft to body weight ratio; SFS: small-for-size; PT: prothrombintime; ATP: adenosine triphosphate

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#### REFERENCES

1. Edwards EB, Harper AM. Application of a continuous disease severity score to the OPTN liver waiting list. Clin Transpl. 2001;19-24. PubMed PMID: 12211782.
2. Poon KS, Chen TH, Jeng LB, Yang HR, Li PC, Lee CC, et al. A high model for end-stage liver disease score should not be considered a contraindication to living donor liver transplantation. Transplant Proc. 2012;44(2):316-319. PubMed PMID: 22410005.
3. Alves RC, Fonseca EA, Mattos CA, Abdalla S, Goncalves JE, Waisberg J. Predictive factors of early graft loss in living donor liver transplantation. Arq Gastroenterol. 2012;49(2):157-161. PubMed PMID: 22767004.
4. Kanwal F, Chen D, Ting L, Gornbein J, Saab S, Durazo F, et al. A model to predict the development of mental status changes of unclear cause after liver transplantation. Liver Transpl. 2003;9(12):1312-1319. PubMed PMID: 14625832.
5. Sorrell JH, Zolnikov BJ, Sharma A, Jinnai I. Cognitive impairment in people diagnosed with end-stage liver disease evaluated for liver transplantation. Psychiatry Clin Neurosci. 2006;60(2):174-181. PubMed PMID: 16594941.
6. Burkhalter EL, Starzl TE, Van Thiel DH. Severe neurological complications following orthotopic liver transplantation in patients receiving FK 506 and prednisone. J Hepatol. 1994;21(4):572-577. PubMed PMID: 7529272.